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November 26 2003
HETA 2001-0445
Interim Letter IV

Mike Winkler
President
Administrative and Residual Employees Union
705 North Mountain Road, Suite A211
Newington, Connecticut 06111

Dear Mr. Winkler:

This interim letter and attached report are in regards to a health hazard evaluation request from the Administrative and Residual Employees Union Local 4200 representing office workers at 25 Sigourney Street in Hartford, Connecticut. The attached interim report (Appendix A) contains the results of data analysis of the medical questionnaire and testing carried out June 3-14, 2002. Most of the information in this interim report was presented at an update meeting for stakeholders held in August 2003 at the Sigourney Street building. During the August update meeting, EH&E (NIOSH contractor) presented results of fungal sampling carried out in the Sigourney Street building during May 2003, as well as a brief overview of findings relating to building ventilation, pressurization and visual inspection of the HVAC system. All stakeholders gave brief updates of information.

In summary, the findings from our medical survey and data analyses are as follows:

1) The participants with symptoms in June 2002 had more abnormal lung function tests results as well as more medication use for breathing problems than the asymptomatic (comparison group) participants.
2) In participants from both agencies, working on a number of floors in the building, there was evidence for new onset of symptoms or exacerbation of preexisting asthma in the seven-month period from September 2001 and June 2002.
3) The top five ranked floors for prevalence of abnormal medical results, symptoms or medication use in symptomatic participants were floors 14, 19, 10, 6 and 17.
4) There was no statistical difference in the prevalence of atopy or being skin prick positive to the mold mixes between the symptomatic and asymptomatic participants.
5) Overall, the mean values for the markers of inflammation were not statistically different between symptomatic and asymptomatic participants. However, in the never smokers, participants with current physician-diagnosed asthma had a statistically higher prevalence of exhaled nitric oxide (eNO) values of 9 ppb or higher.

Taking into account information presented at the August, 2003 stakeholder meeting, we conclude that:

1) The results of the June 2002 medical survey substantiated the reporting of symptoms by the occupants of the Sigourney Street building.
2) The building environment had posed some risk to previously unaffected occupants between September 2001 and June 2002.

3) This finding, combined with the presence of current symptoms in June 2002, abnormal respiratory function, and breathing medication use, validated the need for the ongoing continued attention to building remediation and the health concerns of building occupants.
4) We have some indications from objective testing that the building environment is improving in 2003 in relation to dampness and possible fungal contamination, but we do not have questionnaire or medical survey data from this time frame.
5) We plan that a follow-up survey be carried out in the summer of 2004, some months after the remediation and construction has been completed to help document the effect of building remediation on employee health.

If you have any questions regarding the information provided in this interim letter and attached report, please do not hesitate to contact us at 1-800-232-2114.

Sincerely,

Jean Cox-Ganser, Ph.D.
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APPENDIX A:

INTERIM REPORT ON THE JUNE 2002 MEDICAL SURVEY AT THE SIGOURNEY STREET BUILDING HETA 2001-0445 NOVEMBER 26, 2003

Background

On July 17, 2001, the National Institute for Occupational Safety and Health (NIOSH) received a health hazard evaluation request from the Administrative and Residual Employees Union Local 4200 representing office workers at 25 Sigourney Street in Hartford, CT. Workers reported respiratory and dermatological conditions that they perceived to be building-related. Symptom onset spanned several years with an increase in symptoms and frequency of complaints since the fall of 2000. There has been documented post-hire onset of asthma, hypersensitivity pneumonitis (HP), and sarcoidosis with these employees being relocated to another facility.

The building houses two state agencies: the CT Department of Revenue Services (DRS) and the Department of Social Services (DSS). Approximately 1,300 people work in the building. The building is owned by the State and managed by the Tunxis group for the Department of Public Works (DPW).

The facility is a 20-floor building with parking garages on the bottom four floors and a lobby/cafeteria/mezzanine area on the 5th floor. A history of water damage exists on the upper floors of the building. Currently, remediation of the building envelope, interior water-damaged wallboard, and carpet is underway.

NIOSH conducted a site visit from September 11-14, 2001, to administer a short health questionnaire offered to all employees. The results of this questionnaire were provided in an interim letter on January 28, 2002. NIOSH staff returned to the Sigourney Street facility June 3-14, 2002, to conduct medical testing and to administer a questionnaire.

Objectives of the June 2002 medical survey

This report presents the results of the June 2002 medical survey. The report focuses on seven topics:

1. Do the results of the medical survey substantiate the employee reports of lower respiratory symptoms and conditions?
2. Was there evidence of onset of respiratory conditions in the previously asymptomatic participants over the seven-month period between surveys?
3. On what floors of the building did onset of symptoms occur?
4. Was there any evidence that symptomatic participants from different floors had differences in medical test results and medication use?
5. What was the usefulness of our medical testing for individual employees?
6. Summarize results for the skin prick allergy tests.

7. Summarize results for the newer tests for inflammation of the lungs.

Invitation to participate in the June 2002 medical survey

Since we lacked the resources to offer the medical survey to all employees, we applied a lower respiratory case definition and a comparison (or asymptomatic group) definition (as shown below) to the results of the September 2001 questionnaire. We invited the 202 employees who met the case definition and the 154 employees who met the comparison group definition to participate in the June 2002 survey. Employees in both groups must have worked in the Sigourney Street building for at least one year to be included.

Respiratory case definition:

- three or more of five lower respiratory symptoms (wheeze/whistling in the chest, chest tightness, shortness of breath, coughing, awakened by attack of breathing difficulty) occurring weekly over the past month;
  OR
- two or more of three symptoms consistent with hypersensitivity pneumonitis (HP) (shortness of breath when hurrying on level ground or walking up a slight hill, fever and chills, flu-like achiness or achy joints) occurring weekly over the past month;
  OR
- current asthma which had been doctor-diagnosed after occupancy of the building,
  OR
- doctor-diagnosed HP or sarcoidosis.

Comparison group definition:

- none of the above listed lower respiratory or HP-like symptoms in the past year,
  AND
- none of the diagnoses listed for the symptomatic group.

Participation in the June 2002 survey

Before the medical survey, NIOSH emailed invitees an explanation of the medical tests offered as well as the consent form. NIOSH staff visited the Sigourney Street building in May 2002 to meet with invited employees, explain the medical tests, and to conduct the informed consent procedure with employees who accepted the invitation to participate in the medical survey. During the two-week survey in June, invited employees, who had not been available in May, were contacted and went through the informed consent procedure before survey participation.

A total of 248 employees participated in the survey, including 142 (70%) of the 202 respiratory cases and 91 of the 154 (59%) comparison group employees. An additional 15 employees requested testing during the June visit. Not all participants completed each of the different medical tests. Demographics of the participants are shown in Table 1.

Table 1. June 2002 participation in survey and demographics of participants

	Respiratory cases in September 2001	Comparison group in September 2001	Volunteers
Participation	142/202 70%	91/154 59%	15 N/A
Women	71%	49%	60%
Age in years (mean, ± SD)	47 ± 8	47 ± 9	52 ± 10
Duration of occupancy in years (mean, ± SD)	7 ± 2	7 ± 2	7 ± 3
Current smoker	16%	11%	0%
Former smoker	28%	22%	20%
Never smoker	57%	67%	80%

Medical tests

Introduction

The questionnaire and lung function tests offered were pertinent to the assessment of health effects consistent with asthma, and to some extent with interstitial lung conditions such as hypersensitivity pneumonitis (HP) and sarcoidosis. Asthma and HP have been reported in relation to water-damaged buildings.[1,2] The cause of sarcoidosis is not understood. We also offered some newer tests for inflammation of the lungs (described below). We are evaluating these tests for their usefulness as early markers of inflammation in indoor environmental settings. Lastly, skin prick allergen testing was carried out to assess atopy, which is sensitization to "common allergens" such as house dust mite, pet, pollen, grasses, trees, weeds, and cockroach. Atopy has been reported in the literature as a risk factor for asthma.[3,4]

People with asthma typically have symptoms of episodic wheezing, chest tightness, shortness of breath, and/or a chronic cough. When these symptoms become worrisome, people usually seek medical attention. Their physicians may then make an asthma diagnosis, prescribe an inhaled corticosteroid (an asthma controller medication to reduce airway inflammation), and prescribe a beta-agonist inhaler (a rescue medication to quickly open airways). When an allergy trigger worsens or exacerbates the patient's asthma, an oral corticosteroid (such as prednisone) is often prescribed for a week or two.

When asthma is poorly controlled and the patient has daily respiratory symptoms, spirometry will usually show airway obstruction. Ten minutes after the patient inhales a bronchodilator (albuterol), the obstruction is at least partially relieved – this is called a bronchodilator response.

This pattern of obstruction (or a mixed pattern) with a bronchodilator response is usually due to asthma.

A patient with a history of asthma-like symptoms, but who, at the time of testing, is not in a state of exacerbation of the condition, will often have normal spirometry results. A more sensitive test for underlying asthma can then be done -- a methacholine challenge test (MCT). A MCT result of bronchial hyper-responsiveness (BHR) indicates "twitchy airways," which is consistent with asthma.

Recent medical research suggests that airway inflammation caused by asthma often results in abnormally high concentrations of nitric oxide (NO) and cytokines in the exhaled breath.[5, 6] Cytokines are chemical messengers that the body uses to enhance inflammation.

HP is an immune system response of the lung tissue to repeated inhalation of a variety of sensitizing agents (called antigens), including organic dusts (including molds) and, less often, simple chemicals. Many times the contaminating antigens have been found in water sources in the home or at work.[7] The clinical manifestations of HP are variable, and may be of acute, subacute, or chronic form.[8, 9] In the acute form, flu-like symptoms such as malaise (generally feeling sick with a lack of energy), fever, and chills are typical, with cough, chest-tightness and shortness of breath being common. Pulmonary function changes are typically restrictive (a low vital capacity). Between the flu-like episodes, all medical tests may be normal. In the subacute and chronic forms of HP, the classic symptoms are shortness of breath on exertion, chest tightness, cough (often with sputum production), fatigue, and weight loss.

Sarcoidosis is a disease of unknown cause which can affect many different organs. When it affects the lungs, it may be difficult to differentiate from hypersensitivity pneumonitis. Both diseases result in the same type of granulomatous inflammation and scarring.

Tests Offered

Questionnaire

Contracted, trained interviewers administered a computer-based comprehensive questionnaire to participants. The questionnaire included sections on demographics, work history, health and symptom history, physician diagnoses, breathing medication use, smoking, home environment, and quality of life.

Spirometry

Qualified technicians followed standard guidelines for spirometry.[10] The test results were compared to expected values for a healthy, nonsmoking person of the same age, height, sex, and race using spirometry reference values and 95% normal confidence intervals generated from the third National Health and Nutrition Examination Survey (NHANES III).[11]

We measured forced vital capacity (FVC), the volume of air forcefully exhaled from a maximal inspiration to a complete exhalation; and forced expiratory volume in one second (FEV_1), the

volume of air exhaled in the first second of the forced expiration. The ratio between the two (FEV_1/FVC) was computed. The spirometry breathing test is used to detect narrowing (obstruction) of the airways in the lungs, which occurs with asthma and chronic obstructive pulmonary disease; or the inability to take a deep breath (restriction), which occurs in hypersensitivity pneumonia (HP) and other disorders. Abnormal test results were categorized as having a pattern suggesting obstruction, restriction, or a "mixed" pattern of both airway obstruction and a low FVC.[10] We defined airways obstruction as a low forced expiratory volume in one second to forced vital capacity ratio (FEV_1/FVC%) with low FEV_1. We defined restriction as a low FVC and normal FEV_1/FVC%.

Methacholine Challenge Test (MCT)

The MCT measures the presence and degree of non-specific BHR. To detect BHR, MCT was performed using standardized techniques[12] with five different doses (0.125, 0.5, 2.0, 8.0, and 32.0 milligrams per milliliter (mg/mL)) of methacholine. Five breaths of nebulized methacholine were administered for each dose, starting with 0.125 mg/mL, and spirometry was measured after the fifth breath. If the highest FEV_1 after any dose was greater than 80% of the highest baseline FEV_1, the next higher dose of methacholine was administered. If FEV_1 dropped more than 20% of the baseline value no further methacholine was given. We reported methacholine dose as PC_{20}, which was defined as the provocative concentration of methacholine that caused a 20% or greater decline in FEV_1 from the baseline. Categories of BHR were defined as follows:

PC_{20} less than or equal to 4.0 mg/mL – BHR

PC_{20} between 4.1 and 16.0 mg/mL – borderline BHR

PC_{20} greater than 16 mg/mL – normal

Bronchodilator Administration

In subjects with baseline FEV_1 less than 70% of the predicted value, a bronchodilator was offered to detect any reversible bronchoconstriction instead of undergoing a methacholine challenge test. Two puffs of a beta-agonist were administered via metered dose inhaler and were followed by spirometry. We defined reversibility as a 12% and 200 milliliter FEV_1 improvement after bronchodilator administration.[13]

Exhaled Nitric Oxide (eNO)

Nitric oxide (NO) gas, produced by various cells within the respiratory tract, is detectable in the exhaled air. NO was measured offline using standardized techniques.[14] Exhaled air collected in balloons (Sievers model 01410, Boulder, CO) was analyzed with a rapid-response chemiluminescence analyzer (Sievers model 280; Boulder, CO) for NO level. The upper limit of normal exhaled NO (eNO) has not yet been established. For this report we compare mean levels between participants based on symptomatic status. We also used a cut-off point of 9 parts per billion (ppb) or greater as higher than normal.

Exhaled Breath Condensate (EBC)

EBC testing was being evaluated as a noninvasive way of measuring inflammation in the airways. EBC was collected over a 15-minute period from subjects using previously published techniques.[15] Subjects were asked to perform normal tidal breathing into a disposable cold trap-collection device consisting of a coil of corrugated respiratory tubing (Corr-A-Flex II, Hudson Respiratory Care, Inc., Temecula, CA) submerged into a -15 degree C bath of 50% ethylene glycol. Vapor in the exhaled breath condenses on the cold tubing. The 1-3 milliliters of condensate were collected in vials and stored on dry ice until transfer to the laboratory. Materials carried out of the airways in the exhaled water can then be measured. We measured interleukin-8 (IL-8) and nitrite in the exhaled breath, which may represent biomarkers of pathological processes in the lungs.[16] Nitrite was measured per manufacturer's recommendations using an ozone chemiluminescence NO analyzer (Model 280, Sievers, Boulder, CO). Efforts were initially made to measure IL-8 using a multiplex bead array assay (Upstate, Waltham, MA) with assay results determined using a Luminex-100 reader (Luminex, Austin, TX). Unfortunately, this method had insufficient sensitivity to measure the low levels of IL-8 present in most samples. Thus, samples were re-assessed for IL-8 content using a chemiluminescent immunoassay (QuantiGlo, R & D Systems, Minneapolis, MN) that proved to have adequate sensitivity for the measurements.

The analysis of EBC for airway inflammation markers is still under development and being actively researched in the scientific community. No standardized methods for analysis or setting of cut-off points between normal versus abnormal levels currently exist. In this report we compare mean values between groups of participants based on symptomatic status.

Skin Prick Testing

Skin prick allergy testing was done with commercially available extracts of seven common indoor and outdoor allergens: dust mite mix, German cockroach, cat hair, grass mix, ragweed mix, common weed mix, and Eastern tree mix. In addition, we tested for sensitivity to three commercially available mold mixes: *Alternaria* and *Cladosporium; Aspergillus*; and *Penicillium*. The concentration of each antigen was standardized and selected to produce a rather small skin reaction, or wheal, (about ½ inch in diameter) if a patient was allergic to that antigen. The Greer DermaPIK method was used for the skin allergy testing. The Greer DermaPIK is a plastic, single use device with six tiny tines arranged at the tip in a 2mm circle for epicutaneous allergy skin testing. The allergens were placed on the forearm of the subject, along with a positive (histamine) and negative control (glycerin in water). After 15 minutes, each response wheal length and width was measured to the nearest millimeter and recorded. For each wheal, the mean diameter (average of the length and width) was calculated. A positive reaction to an allergen was defined as an average diameter at least 3mm larger than the negative control and greater than 25% of the average diameter of the positive control. For the purposes of this study, atopy was defined as at least one positive skin test on allergy testing, using a total of seven common antigen extracts (excluding the mold mixes).

Results

Participant reported respiratory status in June 2002

Because changes in invited employees' conditions may have occurred in the time between the September 2001 survey and the medical survey in June 2002, we used the results of the June 2002 questionnaire to reclassify the participants based on the respiratory case and comparison group (i.e. asymptomatic) definitions.
Of the 142 participants originally meeting the respiratory case definition, there were 115 (81%) who continued to meet this classification in June 2002; three (2%) who had become asymptomatic in June 2002; and 24 (17%) who still reported some symptoms but not at the level to meet the respiratory case definition.

Of the 91 participants meeting the comparison group definition in September 2001, 40 (45%) were still asymptomatic in June 2002; 15 (17%) now met the respiratory case definition; and 35 (38%) reported some symptoms, but not at the level to meet the respiratory case definition. One participant had missing information and could not be classified.

Of the 15 participants who asked to take part without a prior NIOSH invitation, ten had taken part in the September 2001 survey but not met either the respiratory case definition or the asymptomatic definition, which meant that they had reported some symptoms. Of these ten participants in both surveys, six now met the respiratory case definition in June 2002. Considering all 15 volunteers in June 2002, ten met the respiratory case definition, one was asymptomatic, and four reported some lower respiratory or systemic symptoms.

Do the results of the medical survey substantiate the employee reports of lower respiratory symptoms and conditions?

We found that the participants with symptoms in June 2002 had more abnormal lung function tests results as well as more medication use for breathing problems than the asymptomatic (comparison group) participants. We also found that the participants who met the respiratory case definition had a higher proportion of abnormal medical tests and more breathing medication use than the group of participants reporting fewer symptoms in June.
In the first analysis shown (Tables 2 and 3), we combine participants who met the respiratory case definition with those reporting any symptoms into one group totaling 203 and contrast them with the 44 asymptomatic participants. For these analyses, the 15 self-selected participants will be included. Since not all participants did all the medical tests, the totals in the tables are less than 203 and 44.

Table 2. Breathing test results for all participants reporting symptoms compared to those not reporting symptoms in the June 2002 survey

Variable	Group with symptoms in June 2002	Comparison group (asymptomatic in June 2002)	p-value
Spirometry testing			
Normal	80% (154/193)**	93% (39/42)	0.045 (Pearson chi-square test)
Abnormal			
Obstructed	9% (18/193)	7% (3/42)	
Restricted	8% (15/193)	0% (0/42)	
Mixed (obstructed and restricted)	3% (6/193)	0% (0/42)	
Invalid	1% (2/195)	None	
% Predicted FEV_1 (Mean ± SD)	93% ± 16	103 ± 12	0.0002 (t-test)
% Predicted FVC (Mean ± SD)	95% ± 15	103 ± 11	0.0012 (t-test)
Methacholine challenge testing			
≤ 4 mg/ml (BHR)	7% (10/150)	0% (0/36)	
> 4 and ≤ 16 mg/ml (borderline BHR)	13% (19/150)	6% (2/36)	
> 16 mg/ml (normal)	81% (121/150)	94% (34/36)	
Bronchodilator testing positive	18% (2/11)	None done	
Abnormal methacholine challenge or bronchodilator tests	19% (31/161)	6% (2/36)	0.047 (Pearson chi-square test)
Any abnormal lung function test*	36% (60/169)	11% (4/37)	0.003 (Pearson chi-square test)

* Participants who had either a negative spirometry, a negative methacholine/bronchodilator test, and who had not done the other tests were excluded.

** The two invalid tests were not included in the denominator.

Table 3. Medication usage and combined medication use and lung function tests for all participants reporting symptoms compared to those not reporting symptoms in the June 2002 survey

Variable	Group with symptoms in June 2002	Comparison group (asymptomatic in June 2002)	Pearson chi-square test p-value
Any medication for breathing problems	36% (73/203)	2% (1/44)	<0.0001
Oral steroids use	17% (34/203)	2% (1/44)	0.013
Inhaled steroid use	14% (28/203)	0% (0/44)	0.009
Beta-agonist use (in the past four weeks)	20% (40/236)	0% (0/42)	0.001
Positive for any medication for breathing problems or abnormal lung function tests	58% (104/179)	11% (4/37)	<0.0001

Stratification of results by smoking category

There were 10% more current or former smokers in the participants reporting symptoms in June 2002 than in the asymptomatic group. The smoking prevalence for participants with and without symptoms was respectively, 14% versus 9% current smokers and 26% versus 21% former smokers.

We see that the reporting of symptoms is supported by the lung function test results and medication use within all smoking categories (Tables 4 and 5). Furthermore it is evident that the reporting of symptoms, breathing medication use and lung function abnormalities occur in the participants who reported never having smoked, showing that smoking does not account for all the respiratory health issues of the participants.

Overall, current and former smokers had a trend for more obstruction (a mixed pattern included as obstruction) than never smokers (18%, 15%, and 9% respectively). Although they are not statistically significant at $\alpha < 0.05$, former smokers had more restriction ($p < 0.05$ Pearson chi-square) than never or current smokers (14%, 4%, and 4%).

Table 4. Results of current, former, and never smoker lung function tests

Variable	Current smoker		Former smoker		Never smoker	
	Group with symptoms in June 2002	Comparison group (asymptomatic in June 2002)	Group with symptoms in June 2002	Comparison group (asymptomatic in June 2002)	Group with symptoms in June 2002	Comparison group (asymptomatic in June 2002)
Spirometry testing	79% (19/24)	75% (3/4)	67% (34/51)	100% (8/8)	86% (101/118)	93% (28/30)
Normal						
Abnormal	13% (3/24)	25% (1/4)	12% (6/51)	0% (0/8)	8% (9/118)	7% (2/30)
Obstructed	4% (1/24)	0% (0/4)	16% (8/51)	0% (0/8)	5% (6/118)	0% (0/30)
Restricted	4% (1/24)	0% (0/4)	6% (3/51)	0% (0/8)	2% (2/118)	0% (0/30)
Mixed	4% (1/25)	0% (0/4)	2% (1/52)	0% (0/8)	0% (0/118)	0% (0/30)
Invalid**						
% Predicted FEV_1 (Mean ± SD)	90% ± 11	99% ± 14	88% ± 20	108% ± 12	96% ± 15	103% ± 11
% Predicted FVC (Mean ± SD)	93% ± 8	100% ± 8	89% ± 17	106% ± 14	98% ± 14	102% ± 10
Methacholine challenge testing						
≤ 4 mg/ml (BHR)	0% (0/22)	0% (0/2)	10% (4/40)	0% (0/8)	7% (6/88)	0% (0/26)
> 4 and ≤ 16 mg/ml (borderline BHR)	14% (3/22)	0% (0/2)	10% (4/40)	0% (0/8)	14% (12/88)	8% (2/26)
> 16 mg/ml (normal)	86% (19/22)	100% (2/2)	80% (32/40)	100% (8/8)	80% (70/88)	92% (24/26)
Bronchodilator testing positive	0% (0/1)	None done	0% (0/3)	None done	29% (2/7)	None done
Abnormal Methacholine challenge or bronchodilator tests	13%(3/23)	0% (0/2)	19%(8/43)	0% (0/8)	21% (20/95)	8% (2/26)
Any abnormal lung function test*	30% (7/23)	33% (1/3)	48% (22/46)	0% (0/8)	31% (31/100)	12% (3/26)

* Participants who had either a negative spirometry, a negative methacholine/bronchodilator test, and who had not done the other tests were excluded.

** Invalid tests were not included in the denominator.

Table 5. Medication usage and combined medication use and lung function tests for current, former, and never smokers

Variable	Current smokers		Former smokers		Never smokers	
	Group with symptoms in June 2002	Comparison group (asymptomatic in June 2002)	Group with symptoms in June 2002	Comparison group (asymptomatic in June 2002)	Group with symptoms in June 2002	Comparison group (asymptomatic in June 2002)
Any medication for breathing problems	29% (8/28)	25% (1/4)	36% (19/53)	0% (0/9)	38% (46/122)	0% (0/31)
Oral steroids use	14% (4/28)	25% (1/4)	23 % (12/53)	0% (0/9)	15% (18/122)	0% (0/31)
Inhaled steroid use	7% (2/28)	0% (0/4)	21% (11/53)	0% (0/9)	12% (15/122)	0% (0/31)
Beta-agonist use (in the past four weeks)	11% (3/28)	0% (0/4)	23% (12/53)	0% (0/9)	21% (25/122)	0% (0/31)
Positive for any medication for breathing problems or abnormal lung function tests	52% (13/25)	33%% (1/3)	65% (31/48)	0% (0/8)	57% (60/106)	12% (3/26)

There was evidence for a gradient in the medical test results and the use of breathing medication in relation to level of symptom reporting in June 2002. We found that participants meeting the respiratory case definition in June had the highest proportion of abnormal medical tests and higher medication use. This trend was clear in the never smoker participants, where the prevalence of abnormal lung function tests and medication use was 71%, 30% and 12% for respiratory cases, participants with fewer symptoms and the asymptomatic group respectively (Tables 6 and 7).

Table 6. Never smokers lung function results stratified by level of symptoms

Variable	Respiratory cases	Group with fewer symptoms	Asymptomatic comparison group
Pulmonary function testing			
Normal	80% (60/75)	95% (41/43)	93% (28/30)
Abnormal			
Obstructed	9% (7/75)	5% (2/43)	7% (2/30)
Restricted	8% (6/75)	0% (0/43)	0% (0/30)
Mixed	3% (2/75)	0% (0/43)	0% (0/30)
% Predicted FEV_1 (Mean ± SD)	94% ± 16	101% ± 12	103% ± 11
% Predicted FVC (Mean ± SD)	95% ± 15	101% ± 11	102% ± 10
Methacholine challenge testing			
≤ 4 mg/ml (BHR)	6% (3/52)	6% (2/36)	0% (0/26)
> 4 and ≤ 16 mg/ml (borderline BHR)	17% (9/52)	11% (4/36)	8% (2/26)
> 16 mg/ml (normal)	77% (40/52)	83% (30/36)	92% (24/26)
Bronchodilator testing positive	29% (2/7)	None done	None done
Abnormal Methacholine challenge or bronchodilator tests	24% (14/59)	17% (6/36)	8% (2/26)
Any abnormal lung function test*	38% (24/63)	19% (7/37)	12% (3/26)

* Participants who had either a negative spirometry, a negative methacholine/bronchodilator test, and who had not done the other tests were excluded.

Table 7. Medication usage and combined medication use and lung function tests for never smokers stratified by symptom level.

Variable	Respiratory cases	Group with fewer symptoms	Asymptomatic comparison group
Any medication for breathing problems	50% (39/78)	16% (7/44)	0% (0/31)
Oral steroids use	18% (14/78)	9% (4/44)	0% (0/31)
Inhaled steroid use	18% (14/78)	2% (1/44)	0% (0/31)
Beta-agonist use (in the past four weeks)	31% (24/78)	2% (1/44)	0% (0/31)
Positive for any medication for breathing problems or abnormal lung function tests	71% (49/69)	30% (11/37)	12% (3/26)

Was there evidence of onset of respiratory conditions in the previously asymptomatic participants between surveys?

There was evidence for new onset of symptoms or exacerbation of preexisting asthma in the seven-month period from September 2001 to June 2002. Cough and flu-like achiness or joint pains were predominant (Table 8).

Table 8. Symptom prevalence for 50 of 91 participants who changed from asymptomatic in September 2001 to meeting the respiratory case definition or reporting some symptoms in June 2002

Variable	From asymptomatic to respiratory case	From asymptomatic to some symptoms
Asthma-like symptoms during last four weeks:		
Sleep broken by difficulty with breathing	40% (6/15)	3% (1/35)
Cough	73% (11/15)	63% (22/35)
Wheezing	33% (5/15)	3% (1/35)
Shortness of breath	47% (7/15)	9% (3/35)
Chest tightness	20% (3/15)	9% (3/35)
HP-like symptoms during last four weeks:		
Fever or chills	27% (4/15)	3% (1/35)
Flu-like achiness or joint pain	87% (13/15)	29% (10/35)
Shortness of breath while walking on level ground	60% (9/15)	17% (6/35)

Fifteen of the 91 participants who had been asymptomatic in September 2001 met the respiratory case definition in June 2002. All 15 met this definition by symptom criteria and not by reporting physician diagnosis of asthma, HP, or sarcoidosis during the seven months. Nine of the 15 met the definition by reporting HP-like symptoms, four by lower respiratory symptoms, and two by both HP-like and lower respiratory symptoms. Two participants had reported physician-

diagnosed asthma that was not current in September 2001; however, in the June 2002 questionnaire, they indicated their asthma was current. Twenty percent of this group had an abnormal pulmonary function test, and one individual had borderline BHR (Table 9). Twenty percent of the 15 reported the use of breathing medication (Table 10). There were 20% current smokers and 20% former smokers in this group of 15.

The remaining 35 participants who were asymptomatic in September 2001, reported lower respiratory and/or HP-like symptoms in June 2002, however not at a level to meet the respiratory case definition. Eight percent of their pulmonary function tests showed an abnormal pattern (Table 9). Seven percent of these individuals had borderline bronchial hyperresponsiveness, and six percent of this group reported using medication for their breathing (Table 10). There were 11% current smokers and 23% former smokers in this group of 35.

Table 9. Breathing test results for 50 of 91 participants who changed from asymptomatic in September 2001 to reporting symptoms in June 2002

Variable	From asymptomatic to respiratory case	From asymptomatic to some symptoms
Pulmonary function testing		
Normal	73% (11/15)	92% (32/35)
Abnormal		
Obstructed	7% (1/15)	6% (2/35)
Restricted	13% (2/15)	3% (1/35)
Mixed	0% (0/15)	0% (0/35)
Invalid**	7% (1/15)	0% (0/35)
% Predicted FEV_1 (Mean + SD)	94% ± 15	96% ± 17
% Predicted FVC (Mean ± SD)	95% ± 15	96% ± 16
Methacholine challenge testing		
≤ 4 mg/ml (BHR)	0% (0/11)	0% (0/27)
> 4 mg/ml and ≤ 16 mg/ml (borderline BHR)	9% (1/11)	7% (2/27)
>16 mg/ml (normal)	91% (10/11)	93% (25/27)
Bronchodilator testing positive	None done	None done
Any abnormal lung function test*	25% (3/12)	17% (6/29)

* Participants with either negative spirometry or methacholine/bronchodilator test, but the other test not done were excluded.

** Invalid tests were not included in the denominator.

Table 10. Medication usage and combined medication use and lung function tests for 50 of 91 participants who changed from asymptomatic in September 2001 to reporting symptoms in June 2002

Variable	From asymptomatic to respiratory case	From asymptomatic to some symptoms
Any medication for breathing problems	20% (3/15)	6% (2/35)
Oral steroids use	7% (1/15)	6% (2/35)
Inhaled steroid use	7% (1/15)	0% (0/35)
Beta-agonist use (in the past four weeks)	20% (3/15)	0% (0/35)
Positive for any medication for breathing problems or abnormal lung function tests	42% (5/12)	24% (7/29)

On what floors of the building did onset of symptoms occur?

The 15 formerly asymptomatic participants who met the respiratory case definition in June 2002 worked for both agencies, with 9/15 (60%) employed by DRS and 6/15 (40%) employed by DSS. These employees worked on many different floors of the Sigourney Street building from the 5th floor to the 19th floor. The 35 participants reporting new onset of some symptoms also worked for both agencies: 17/35 (49%) for DRS and 18/35 (51%) for DSS. All floors from the 5th to the 19th were represented.

Was there any evidence that symptomatic participants from different floors had differences in medical test results and medication use?

There was some indication of differences across the floors in medical test results for the symptomatic participants. The asymptomatic participants, and the symptomatic participants not working in the Sigourney Street building at the time of the survey or for whom we had missing work floor information in June 2002 were excluded from this analysis. For the symptomatic participants, we compared the prevalence of work-related symptoms, abnormal spirometry results, and BHR across the floors. We created a severity scale for symptoms and medication use based on the June 2002 questionnaire, and for each participant applied these severity scales to the questionnaire responses. We compared the mean values for these symptoms and breathing medication use scores.

The top five ranked floors for the abnormal medical results, symptoms or medication use are presented (Table 11). We see that floors 14 and 19 are ranked in the top five for all or most of the outcomes, while floors 10, 6 and 17 are ranked in the top five for at least three of the outcomes. This information may help in focusing a check of possible exposure sources on these floors, although all floors should be considered.

Table 11. Ranking of floors in regards to distribution of medical survey results in the symptomatic participants in June 2002

Result category	Rank*				
	1	2	3	4	5
Work-related respiratory symptoms	19th	18th	14th	10th	17th
Symptom Score	19th	14th	18th	6th	10th
Medication Score	19th	14th	10th	6th	17th
Obstruction/Mixed	12th	14th	5th	9th	16th
Restriction	19th	14th	10th	6th	17th
Methacholine/Bronchodilator	19th	11th	9th	14th	16th

* Employees relocated out of the Sigourney Street building at the time of the medical survey were excluded from this analysis.

What was the usefulness of our medical testing for individual employees?

In August 2002, each participant in the medical testing received written notification of his/her own results. When participants had abnormal test results they were advised to consult their own doctors for further follow-up.

Amongst those advised to consult their doctors were 34 participants who reported that they were taking no medication for breathing problems yet had some lung function abnormality on the survey tests. Three of these employees also did not report symptoms. These participants may have been unaware of any respiratory health conditions. The spirometry results indicated both obstructive and restrictive abnormalities. A number of these participants had evidence of twitchy airways, with four showing BHR and another 12 with borderline BHR.

Summary results for the skin prick allergy tests.

Over half of the participants met the definition for being atopic, in that they had at least one out of seven positive responses to common indoor and outdoor allergens. There were fewer participants positive to the three mold mixes (Table 12). There was no statistical difference in the prevalence of atopy or being positive to the mold mixes between the symptomatic and asymptomatic participants or between participants with and without physician-diagnosed asthma. Physician-diagnosed asthma was associated with a positive skin prick test for cat allergen ($p < 0.01$).

Table 12. Skin prick allergy test results by symptomatic status and physician diagnosed asthma in the June 2002 survey

Variable	Symptomatic n=180	Asymptomatic n=39	Physician-diagnosed asthma n=63	No asthma n=157
Dust mite mix	29%	26%	25%	29%
Cat	27%	15%	38%**	19%
Cockroach	12%	13%	11%	13%
Tree mix	24%	26%	25%	24%
Grass mix	23%	26%	22%	24%
Weed mix	16%	18%	21%	14%
Ragweed	22%	21%	24%	21%
Atopic*	57%	54%	60%	55%
Mold mixes				
Penicillium	7%	8%	3%	8%
Alternaria/Cladosporium	11%	8%	5%	13%
Aspergillus	10%	8%	8%	10%
Any one or more mold mix positive	18%	13%	11%	20%

* Positive response to one or more of seven common allergens.

** Comparison between physician-diagnosed asthma and no asthma groups, statistically significant at $p < 0.01$ (Pearson chi-square).

Newer tests for inflammation of the lungs.

The mean values for the eNO, IL-8 and nitrites in the exhaled breath condensate did not indicate any differences in the mean values between symptomatic and asymptomatic participants (Table 13). When the results were stratified by smoking category, the eNO levels were higher in non-smoking symptomatic participants, but not statistically significant. The eNO results did not correlate well with the methacholine challenge/bronchodilator tests in the non-smokers, with 19% of the normal lung function tests and 24% of the abnormal tests having eNO values of 9 ppb or more. In the never smokers, we found that reporting current physician diagnosed asthma was positively and significantly (Pearson chi-square $p < 0.02$) associated with eNO values of 9 ppb or higher. The prevalence of high nitric oxide was 33% in the asthmatics and 15% in the rest of the never smokers.

Table 13. Biomarkers of inflammation results for all participants reporting symptoms compared to those not reporting symptoms in the June 2002 survey

Variable	Symptomatic current smokers	Asymptomatic current smokers	Symptomatic former/never smokers	Asymptomatic former/never smokers
eNO (ppb, Mean ± SD)	5 ± 2	5 ± 3	7 ± 4	6 ± 2
eNO (≥ 9 ppb)	4% (1/27)	25% (1/4)	22% (36/166)	11% (4/38)
IL-8 (pg/ml, Mean ± SD)	2.8 ± 0.9	2.8 ± 0.7	3.7 ± 4.5	2.8 ± 0.9
Nitrite (μmol, Mean ± SD)	1.0 ± 1.2	0.8 ± 0.2	0.9 ± 1.2	0.7 ± 0.5

Discussion

Most of the information in this interim report was presented at an update meeting for stakeholders held in August 2003 at the Sigourney Street building. As was shown during the presentation, the results of the June 2002 medical survey substantiated the reporting of symptoms by the occupants of the Sigourney Street building. The symptomatic participants showed more lung function abnormalities and breathing medication use and this held true when smoking was taken into account. Further validation of symptom reporting was the presence of a gradient of abnormal lung function and medication use. The most symptomatic participants had the highest levels of objective indications of respiratory problems; the participants reporting fewer symptoms were intermediate; and the asymptomatic participants had the least abnormal lung function tests and medication use. These medical data validate the utility of symptom-based questionnaires in assessing building-related respiratory illness.

Proportionately more participants changed from asymptomatic to symptomatic than vice versa in the nine-month period between surveys. This indicates the building environment had posed continuing risk to previously unaffected occupants during this time. This finding, combined with the presence of current symptoms in June 2002, abnormal respiratory function, and breathing medication use, points to the necessity of the continued attention to building remediation and the health concerns of building occupants. Prior to June 2002, some remediation of water-damaged areas had occurred and a number of employees had been relocated out of the building due to health concerns. The building renovation and construction activities to stop water incursions continued in 2002 and 2003.

Historically, the upper floors of the building had been implicated in having water incursions and employees with building-related health effects. The results of the September 2001 survey had shown that employees from both lower and upper floors were experiencing symptoms. We used the June 2002 survey results to look for indications of possible differences in risk within the building. The respiratory problems with new onset between September 2001 and June 2002 occurred on all floors. This suggests that attention needs to be paid to all floors during the remediation process. Nonetheless, the evidence that in June 2002 symptomatic participants from the 6th, 10th, 14th, 17th, and 19th floors had higher levels of positive lung function tests, work-

related symptoms and breathing medication use indicates that these floors should have some added attention.

During the August update meeting, EH&E (NIOSH contractor) presented results of fungal sampling carried out in the Sigourney Street building during May 2003, as well as a brief overview of findings relating to building ventilation, pressurization and visual inspection of the HVAC system. All stakeholders gave brief updates of information.

The 2003 sampling by EH&E indicated low levels of mold in the air and in wall cavities in comparison to in-wall fungal spore concentrations from sampling carried out by consultants hired by DPW in 1991. In general, the air fungal levels measured by EH&E were not different from those found in the EPA BASE study of non-problem buildings in the U.S (personal communication from EH&E). This was interpreted to indicate that the remediation activities to stop water incursions and remove wetted materials are effective. During the August 2003 update meeting we learned from the agencies that the number of employees reporting building-related health concerns had been low recently. It was reported that in general, employees are more satisfied because remediation and construction activities are now being communicated and containment procedures are improved. Thus there seems to be consistency between the environmental findings and anecdotal employee health concerns, both of which seem to have improved.

The preliminary analysis of the skin prick allergy testing did not indicate that the symptomatic participants had more allergic response to the common allergens used. Thus, allergic disposition appears to have nothing to do with the presence of symptoms in the building occupants. The mold allergens included in the testing were not meant to represent fungal exposures that may have been present in the Sigourney Street building, but rather were used to gather information of the presence of allergies to common outdoor and indoor mold species. The information on atopy and responses to the common molds will be included in further statistical modeling of health outcomes and our environmental measures of fungal contamination.

During the June 2002 medical survey we had included some newer tests for inflammation of the airways in the hopes that they could be used as an early indication of indoor environmental exposure effects on the respiratory system. The preliminary analyses indicate that these newer tests for lung inflammation were not sensitive in distinguishing between symptomatic and asymptomatic participants in June 2002. As previously reported in the literature, we found that smoking lowers exhaled NO values and is of limited use for detecting inflammation of the airways in current smokers.[17, 18] We are interested in offering these tests in a follow-up survey to investigate their usefulness in indicating changes in employees over time between pre- and post-building remediation.

Although we have some indications from objective testing that the building environment is improving in 2003 in relation to dampness and possible fungal contamination, we do not have questionnaire or medical survey data from this time frame. As was discussed in the update meeting of stakeholders in August 2003, we plan a follow-up survey for the summer of 2004, some months after the remediation and construction has been completed to help document the effect of building remediation on employee health.

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